EXHIBIT 16

EXPERT REPORT
DAVID KESSLER, M.D.

269. After $1 billion in Nucynta IR and ER sales through 2014,[557] Janssen sold the rights to Nucynta IR and ER to Depomed in 2015, for $1.05 billion.[558]

270. As discussed below, the marketing messaging utilized by Janssen to promote Nucynta , like those developed by Purdue for OxyContin, overstated its benefits and understated its risks, but also sought to distinguish Nucynta from OxyContin/oxycodone in order to claim market share.

1. Janssen's Marketing Strategy for Nucynta

(a) Covering Acute to Chronic Continuum

271. Nucynta represented Johnson & Johnson's and Janssen's entry into the oral opioids market. It also represented the first "new molecule" centrally-acting opioid analgesic in 25 years, as Janssen's marketing materials asserted.[559]

272. From the outset, Janssen planned to introduce both IR and ER formulations of Nucynta, with their anticipated approvals about one year apart.[560] They were both addressed in the same pre-launch business plans,[561] in which Janssen discussed how the IR formulation would pave the way for the subsequent adoption of the ER formulation by prescribers, allow for coverage of the full spectrum of pain from acute to chronic in one molecule, and thereby give the drug a competitive advantage against OxyContin/oxycodone:

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[556] Nucynta ER Supplemental Approval Letter, August 28, 2012, available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2012/200533Orig1s001ltr.pdf (last visited March 20, 2019)

[557] PPLP003364349.

[558] JAN-MS-00264775.

[559] JAN-MS-00477361 at 4.

[560] JAN-MS-00477361 at 4.

[561] JAN-MS-00443233 ("Tapentadol Business Plan 2008," dated September 2007); JAN-MS-00477361 ("2009 Tapentadol Business Plan Situation Assessment," dated June 2008); JAN-MS-00350627 ("Nucynta (IR and ER) 2010 Business Plan," dated May 2009).

increase efficacy; 2) fewer gastrointestinal ("GI") side effects; and 3) less abuse liability and withdrawal.

293. These were the first three "Key attributes perceived to differentiate [Nucynta] from existing chronic pain medications" identified in an August 2010 Nucynta ER Payer and Physician Research PowerPoint: "Increased tolerability due to lower GI side effects;" "Decreased abuse potential and tamper-resistant properties;" "Dual mechanism of action."[604]

294. These messages were used to differentiate Nucynta from other analgesics, particularly OxyContin/oxycodone. In my opinion, these superiority claims were neither contained in the label nor supported by substantial evidence, and overstated Nucynta's benefits while understating its risks.

(a) Janssen Overstated the Benefits of Nucynta's Mechanism of Action

295. The Nucynta IR and ER labels have stated from the beginning that tapentadol's exact mechanism is unknown. Through 2010, the IR label additionally stated that "its effect is thought to be due to mu-opioid agonist activity and the inhibition of norepinephrine reuptake."[605] As of 2013, this language changed to "Although the clinical relevance is unclear, preclinical studies have shown that tapentadol is a mu-opioid receptor (MOR) agonist and a norepinephrine reuptake inhibitor (NRI). Analgesia in animal models is derived from both of these properties."[606] The latter language has been the language used in the Nucynta ER label since approval.

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[604] JAN-MS-00473858 at 36

[605] Nucynta IR label, 2008, JAN-MS-00445032; Nucynta IR label, 2009, JAN-MS-01249732; Nucynta IR label, 2010, *available at* https://www.accessdata fda.gov/drugsatfda_docs/label/2010/022304s003lbl.pdf (last visited March 20, 2019)

[606] Nucynta IR label, July 2013, JAN-MS-01229368; Nucynta IR label, October 2013, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/022304s014s015lbl.pdf (last visited March 20,2019); Nucynta IR label, December 2016, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/022304s016lbl.pdf (last visited March 20,2019);

296. Prior to launching Nucynta, Janssen identified its purported "unique dual mechanism of action" as a primary means to differentiate the drug from competitors and "disrupt" habitual prescribing. Janssen's launch materials indicated it planned to use this message to suggest that Nucynta had unique efficacy in "mixed" pain, and that it reduced the need for patients to take additional opioids (a characteristic referred to by Janssen as "opioid sparing").

296.1. Janssen's 2008 Tapentadol Business Plan noted that a "Key IR Message" and "Value Proposition" for Nucynta IR was that it was a "Centrally acting analgesic with dual mechanism of action."[607]

296.2. The same 2008 Business Plan stated on a slide entitled "Phase IV Clinical Development Strategies" "Bridge the gap between pre-clinical and clinical perspective regarding MOA--Demonstrate versatility of the molecule in PCP- relevant pain models." The slide suggested that the "Dual MoA" led to greater efficacy and safety.[608]

296.3. The 2008 Business Plan further stated on a "Brand Vision" slide that the dual MOA had "'Opioid Sparing' Effects" which would mean less withdrawal symptoms and less dose escalation.[609] No evidence was cited for these claims.

Nuynta IR label, September 2018, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022304s019s021lbl.pdf (last visited March 20,2019); Nucynta ER label, 2011, JAN-MS-02544901; Nucynta ER label, July 2012, JAN-MS-00229587; Nucynta ER label, August 2012, JAN-MS-00229558; Nucynta ER label, April 2014, JAN-MS-03088328; Nucynta ER label, December 2016, *available at* https://www.accessdata fda.gov/drugsatfda_docs/label/2016/200533s014lbl.pdf (last visited March 20,2019); Nucynta ER label, September 2018, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/200533s018s019lbl.pdf (last visited March 20,2019).

[607] JAN-MS-00443233 at 10.

[608] *Id.* at 11.

[609] *Id.* at 12.

296.4. A September 2008 press release Janssen drafted in anticipation of Nucynta IR's approval stated "Nucynta has a unique profile with two mechanisms of action, combining mu-opioid receptor agonism and norepinephrine reuptake inhibition in a single molecule." [610] In a September, 2008 email chain addressing the draft, Janssen executive Kathleen Dusek stated that based on a review of an FDA warning letter, the word "unique" (among others in the press release) "might be contentious," and went on to assert "We do not have clinical data to support the dual mechanism of action. Generally, FDA feels that preclinical evidence is not enough."[611] The language Dusek identified was removed from the final version of the press release, but the company continued to tout the the benefits of Nucynta's dual MoA in its promotional materials, as noted below.

296.5. In a SWOT analysis in its 2009 Tapentadol Business Plan, Janssen listed among Nucynta's strengths "Dual Mechanism of Actions in 1 molecule," but then listed among its weaknesses "Norepinephrine benefit not clear/quantifiable."[612]

296.6. In its 2009 "Marketing Overview Strategic Plan," Janssen again stated that the drug's "Dual MOA-Opioid Sparing Effects" was a "Value Proposition" that would lead to "less withdrawal symptoms," "less dose escalation (durability)," and "emotional wellbeing."[613] No evidence was cited for these claims.

[610] JAN-MS-01124875 at 2-4.

[611] JAN-MS-01124875.

[612] JAN-MS-00477361 at 19, 20.

[613] JAN-MS-00457581 at slide 10.

296.7. Another slide in the 2009 Plan stated "The μ-opioid-sparing effect message should be emphasized (opiophobia is common in primary care)."[614]

296.8. In a slide in the same 2009 Plan on "Optimizing Analgesic Therapy for Moderate to Severe Pain," Janssen listed an objective of "Highlight recent research supporting the benefits of multi-modal therapy to maximize analgesic efficacy and minimize side effects" in order to "Set the stage for introduction of tapentadol," "An agent with mu-opioid agonist and NE-reuptake inhibition mechanisms of analgesia."[615] No such research was cited.

296.9. In slides in the same 2009 Plan regarding speaker and KOL engagements, unbranded publications, and secondary publications, Janssen's notes to the slides stated these would "Support the rationale for an agent with two MOAs."[616]

296.10. A "Tested Positioning Statement" in the 2009 Plan presented a "The Best of Both Worlds" statement. This statement asserted that Nucynta provided "pain relief without tradeoffs," which was unsupported by substantial evidence:

> Product X [Nucynta] is the only *dual-acting*, single-agent, Schedule II analgesic linking powerful opioid efficacy with unprecedented tolerability that enables physicians to provide *pain relief without tradeoffs* because it *selectively works on both the mu-opioid and norepinephrine pathways for optimal pain control* without treatment-compromising side effects.[617]

296.11. An "APS [American Pain Society] Activities" section of the 2009 Plan indicated that Janssen would be sponsoring an APS booth that would feature several

[614] *Id.* at 41.

[615] *Id.* at 33.

[616] *Id.* at 35, 49, 153.

[617] *Id.* at 89 (emphasis added).

Janssen posters, including one called "Pathways," which stated "Multimodal pathways that address more than one pathway may provide more comprehensive relief." [618]

296.12. Janssen's 2010 Nucynta Business Plan identified as a "lever of growth" "Drive the **mixed / multi-etiology of pain consideration for a broader pain types using the dual MOA followed by DPN findings as the proof of concept and** rational [sic] for first line / foundation of management."[619]

296.13. Two slides later, however, the 2010 Business Plan recognized as a "challenge" the fact that "MOA is a proof of concept only."[620]

296.14. Similarly, a slide in the 2010 Plan listing "Strengths" notes "Dual MOA resonates with mu-receptor sparing effects," but the next slide on "Weaknesses" noted "Norepinephrine benefit not clear/quantifiable."[621]

296.15. Janssen's 2011 Nucynta ER Launch Plan identified "Unique Mechanism of Action" as a "Nucynta ER Core Message," and asserted that "Unlike traditional opioids, Nucynta has 2 proven analgesic mechanisms."[622]

296.16. The 2011 ER Launch Plan also indicated that in a presentation on osteoarthritis data for Nucynta, physicians identified the key message as "A new pain medication with equal or greater efficacy than OxyContin, but fewer side effects, less discontinuation and a dual MOA."[623]

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[618] *Id.* at 54, 65.

[619] JAN-MS-00350627 at 5. (Emphasis in original.)

[620] JAN-MS-00350627 at 7.

[621] JAN-MS-00350627 at 10, 11.

[622] JAN00012142 at 8.

[623] *Id.* at 22.

296.17. A slide entitled "Tapentadol answers the unmet need" in the 2011 Launch Plan contained the position statement that Nucynta is "the only broad coverage analgesic that provides superior outcomes" because… "Dual MOA, (MU/NRI) provide opioid-sparing benefits."[624]

297. Once Nucynta was on the market, Janssen continued to promote the purported "unique dual mechanism of action" of Nucynta as a primary means to differentiate the drug from competitors and "disrupt" habitual prescribing. Janssen's marketing materials falsely suggested that this mechanism imparted to Nucynta unique efficacy in certain types of pain, particularly back and neck pain, and reduced the need for patients to take additional opioids.

297.1. A May 2010 recap of a "Nucynta Ask the Expert Call" for sales representatives shows that in response to a discussion of the norepinephrine mechanism, Janssen suggested that the representatives "d[idn't] need to get into the science" but should ask, "Why would you not use a drug that hits pain from multiple pathways?"[625] In the Nucynta FAQ (Frequently Asked Questions) referred to in the recap, the response to the FAQ of "What is the contribution of analgesia of NUCYNTA through mu-receptor agonism and norepinephrine reuptake inhibition?" is "This is currently being investigated by Grunenthal and at this point we cannot comment."[626]

297.2. In Janssen's 2012 Nucynta and Nucynta ER Business Plan, Janssen laid out a marketing strategy to "generate data to support MoA differentiation" in order to "strengthen differentiation and value through new & compelling evidence."[627]

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[624] *Id.* at 30.

[625] JAN-MS-03007471; JAN-MS-03007472

[626] JAN-MS-03024758; JAN-MS-03024760.

[627] JAN-MS-00010801 at 12, 42.

297.3. A SWOT analysis in the 2012 Business Plan identified among the drug's strengths "New molecular entity (dual MOA)," and among its opportunities "MOA & GI Tolerability benefits more meaningful in chronic pain."[628]

297.4. A "Pain Business Review" for Nucynta IR & ER dated April 23, 2014 contained a "NUCYNTA ER Positioning Statement" asserting that Nucynta "offers a superior overall clinical profile **because**: it provides best-in-class efficacy across multiple pain types… and a unique dual MOA **so that**: physicians and patients can achieve their individualized pain improvement goals without many of the challenges typically associated with traditional opioids."[629] No evidence was cited to support these claims.

297.5. The Review identified among the "RTBs [reasons to believe]" for the Positioning Statement the following: "Dual MOA with mu-opioid agonism and norepinephrine reuptake inhibition."[630]

298. In his deposition, Janssen's former Director of Sales and Marketing, David Lin, testified that the dual mechanism was based solely upon pre-clinical animal studies.[631] He also agreed that "if the exact mechanism of action is unknown, that renders it difficult, if not impossible, to unequivocally make statements about dual mechanism of action."[632]

299. Janssen's sales call notes show that its sales representatives nonetheless frequently promoted Nucynta's "unique" "dual" mechanism of action to healthcare providers,

[628] *Id.* at 61.

[629] JAN-MS-02389698 at 73 (emphasis in original).

[630] *Id.* at 74.

[631] David Lin Dep., 91:12 -95:4 (December 20, 2018).

[632] David Lin Dep., 74:5 -79:12 (December 20, 2018).

without the qualification on the label that the exact mechanism is unknown. The large majority of call notes for Nucynta make these unsupported claims. For example:

299.1. One Illinois call note from July 2009 reports, "I was able to speak with dr Chami about the advantages of having the dual MOA and he told me that he can see how Nucynta would benefit his patients. He also felt that this could keep him from having to use two pain meds for treatment of the back and neck pain patient."[633]

299.2. Another Illinois call note from that same month described speaking "with the dr about the fact that Nucynta Dual MOA and what advantages Nucynta will provide patients that suffer from Back and neck pain."[634]

299.3. A Wisconsin call note from August 2009 states that the sales representative "discussed Nucynta's dual moa and how it could help provide more of a comprehensive approach to pain management, along with comparable efficacy to oxy ir as well as an excellent safety profile makes Nucynta an ideal treatment option to pts with acute pain askd her what her hesitation was in trialing Nucynta, she indicated its newness."[635]

299.4. From 2013 to 2015, "MOA" or "Mechanism of action – Nucynta ER" was listed as the message for 89 sales calls or visits for Nucynta ER.[636]

300. In my opinion, Janssen overstated the benefits of Nucynta's mechanism of action, promoting it as offering increased efficacy and fewer side effects without substantial evidence.

(b) Janssen Overstated the Benefits of Nucynta's GI Tolerability

[633] JAN00118971. Additional call notes can be found in Schedule 11.

[634] *Id.*

[635] *Id.*

[636] JAN00118960.

opioids.[668] The extended release market was dominated by Purdue's OxyContin, which had $2.2 billion in sales in 2008.[669]

309. By the time of Nucynta's approval, there was a growing public health crisis of opioid abuse, particularly of OxyContin/oxycodone, as documented and discussed by many news reports from wide-ranging geographic areas,[670] by FDA in Advisory Committee meetings,[671] by legal filings,[672] and by medical journal articles[673]. As shown below, from early on, Janssen's promotional materials for Nucynta discussed the marketing impact of growing concerns about abuse and turning such concerns to Janssen's advantage. Janssen recognized internally that "increased use is associated with increased abuse and diversion,"[674] but sought to maximize sales of Nucynta while understating the risk of abuse and withdrawal and offering as "solutions" to the abuse problem tools such as its prescriberesponsibly.com website,[675] which minimized the risk of addiction through the concept of "pseudoaddiction."

310. Beginning prior to the approval of Nucynta, Janssen developed marketing plans identifying the medical community's concerns about abuse as a factor in marketing the drug. Those plans sought to allay those concerns, often through understating Nucynta's risk of abuse and withdrawal. At the same time, the plans sought to differentiate Nucynta from

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[668] Opioid sales totals for 2008 calculated from IQVIA (formerly IMS) data reported in PPLP003364349.

[669] *Id.*

[670] *See* PPLPC028000099480; *See also* PDD8107130029; *See also* Borger, Juliana. "Hillbilly Heroin: the Painkiller Abuse Wrecking Lives in West Virginia." The Guardian, 6 June 2001, available at https://www.theguardian.com/world/2001/jun/25/usa.julianborger (last visited March 20, 2019)..

[671] *See* JAN-MS-00616428.

[672] *See* PPLPC018001139508; *See also* PDD1712900150.

[673] *See* PURCHI-000122070; *See also* PURCHI-000241775; *See also* JAN-MS-01466935.

[674] JAN-MS-00771526 at 3.

[675] JAN-MS-00771526 at 31.

317.8. In its 2014 Pain Business Review for Nucynta IR and ER, Janssen claimed that "NUCYNTA ER differentiated on Tolerability and Abuse Potential relative to competition."[705]

317.9. The Pain Business Review contained a "NUCYNTA ER Positioning Statement" asserting that Nucynta "offers a superior overall clinical profile because: it provides best-in-class efficacy across multiple pain types… so that: physicians and patients can achieve their individualized pain improvement goals without many of the challenges typically associated with traditional opioids."[706]

317.10. Despite the fact that by this time FDA had denied Janssen's request for TRF labeling for Nucynta ER, as noted above, the Pain Business Review identified among the "RTBs [reasons to believe]" for the Positioning Statement the following: "Uses technology designed to make it more difficult to crush, split, and dissolve."[707]

317.11. From 2013 to 2015, there were 24 sales calls/visits for Nucynta ER that had "withdrawal" included in the key message.[708]

318. Janssen also understated the risk of addiction and withdrawal from opioids in its unbranded website, prescriberesponsibly.com.

318.1. A piece on the website entitled "Use of Opioid Analgesics in Pain Management," by Keith Candiotti, downplayed the risk of addiction, stating as follows:

> Aside from medical issues related to opioid analgesics, there are nonmedical issues that may have an impact on prescribing patterns and patient use of these drugs. Practitioners are often concerned about

[705] JAN-MS-02389698 at 23.

[706] JAN-MS-02389698 at 73.

[707] JAN-MS-02389698 at 74.

[708] JAN00118960. No narrative is provided for these call notes so the exact nature of what was discussed is unknown.

> prescribing opioid analgesics due to potential legal issues and questions of addiction. By the same token, patients report similar concerns about developing an addiction to opioid analgesics. While these concerns are not without some merit, it would appear that they are often overestimated. According to clinical opinion polls, true addiction occurs only in a small percentage of patients with chronic pain who receive chronic opioid analgesics analgesic therapy.[709]

318.2. A number of materials posted on the website minimized the risk of addiction by invoking the concept of pseudoaddiction. For example, in a piece entitled "What a Prescriber Should Know Before Writing the First Prescription," Heit & Gourlay defined pseudoaddiction as "a syndrome that causes patients to seek additional medications due to inadequate pharmacotherapy being prescribed. Typically when the pain is treated appropriately, the inappropriate behavior ceases."[710]

319. Janssen also financially supported and worked with pain advocacy organizations that put forth "educational" materials and activities that falsely claimed that the risk of opioid addiction had been exaggerated. Below is a brief summary of Janssen's involvement in these advocacy organizations and their false and misleading statements:

319.1. From January 2012 through March 2017 Janssen spent $465,152.85 funding seven different pain advocacy groups.[711] Those groups are: Academy of Integrative Pain Management, American Academy of Pain Management, American

[709] *Id.*

[710] JAN-MS-03090578.

[711] Fueling an Epidemic: Exposing the Financial Ties Between Opioid Manufacturers and Third Party Advocacy Groups. U.S. Senate Homeland Security & Governmental Affairs Committee, Ranking Member's Office, PPLPC031001561047 at 5. Also available at https://www hsgac.senate.gov/imo/media/doc/REPORT-Fueling%20an%20Epidemic-Exposing%20the%20Financial%20Ties%20Between%20Opioid%20Manufacturers%20and%20Third%20Party%20Advocacy%20Groups.pdf

447. In 1997, in a joint publication with the American Academy of Pain Medicine ("AAPM"), APS and AAPM published a guideline titled "The Use of Opioids for the Treatment of Chronic Pain,"[900] containing the following misleading statements regarding opioids:

447.1. "Studies indicate that the de novo development of addiction when opioids are used for the relief of pain is low."[901]

447.2. "[E]xperience has shown that known addicts can benefit from the carefully supervised, judicious use of opioids for the treatment of pain due to cancer, surgery, or recurrent painful illnesses[.]"[902]

447.3. "It is now accepted by practitioners of the specialty of pain medicine that respiratory depression induced by opioids tends to be a short-lived phenomenon, generally occurs only in the opioid-naive patient, and is antagonized by pain. Therefore, withholding the appropriate use of opioids from a patient who is experiencing pain on the basis of respiratory concerns is unwarranted."[903]

447.4. "Furthermore, for most opioids, there does not appear to be an arbitrary upper dosage limit, as was previously thought."[904]

447.5. "The undertreatment of pain in today's society is not justified. This joint consensus statement has been produced pursuant to the missions of both organizations, to help foster a practice environment in which opioids may be used appropriately to reduce needless suffering from pain."[905]

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[900] PPLPC051000030818 at 2.

[901] PPLPC051000030818 at 2.

[902] PPLPC051000030818 at 2.

[903] PPLPC051000030818 at 2.

[904] PPLPC051000030818 at 2.

[905] PPLPC051000030818 at 4.

448. The authors of this guideline included those with ties to opioid manufacturers, including: J. David Haddox, M.D.,[906] David Joranson,[907] Richard Payne, M.D.,[908] and Richard Portenoy, M.D.[909]

449. In the same year that this APS guideline was published, the following manufacturers made the following payments to APS:

449.1. For example, in 1997, Purdue reportedly paid $48,501 and Janssen paid $146,245 to the APS.[910]

449.2. Likewise, Purdue paid $36,800 and Janssen paid $43,500 to the AAPM in 1997.[911]

450. This guideline was used by opioid manufacturers in promoting their opioid products and opioids in general.[912]

2. APS/AAPM/ASAM – Definitions Related to the Use of Opioids for the Treatment of Pain

451. In 2001, APS developed consensus "Definitions Related to the Use of Opioids for the Treatment of Pain" in coordination with AAPM and the American Society of Addiction

[906] At the time, Dr. Haddox was a paid speaker for Purdue. *See*, *e.g.*, PKY180955294 at 1. He was subsequently employed by Purdue as the Vice President of Risk Management and Policy. J. David Haddox Depo. Tr. 57:7-18.

[907] Mr. Joranson is the former director of the University of Wisconsin Pain & Policy Study Group, which was funded by the opioid manufacturers. ENDO-OPIOID_MDL-00658641 at 2-3. The Pain and Policy Study Group also received payments from the manufacturers. See, e.g. ENDO-OR-CID-00754369 at 30, SFC00000001.

[908] At the time, Dr. Payne was a paid speaker for Purdue. *See*, *e.g.*, PKY180256893 at 1, PKY180256892 at 1, PKY180783690 at 1.

[909] At the time, Dr. Portenoy was a paid speaker for Purdue. *See*, *e.g.*, PKY180357269 at 1.

[910] 2012.06.08 Purdue Summary of Payments by Name and Year SFC00000001; J&J Janssen SFC 2012 Submission JAN00000001.

[911] 2012.06.08 Purdue Summary of Payments by Name and Year SFC00000001; J&J Janssen SFC 2012 Submission JAN00000001.

[912] *See, e.g.*, PKY181199494 at 17, 25; PKY181137481 at 8; ALLERGAN_MDL_02158487 at 1; ABT-MDL-KY-0009437 at 54; ENDO-OPIOID_MDL-05967764 at 1.

Medicine ("ASAM"), containing the following misleading statement concerning pseudoaddiction: "An individual's behaviors that may suggest addiction sometimes are simply a reflection of unrelieved pain or other problems unrelated to addiction."[913]

452. In the same year that this 2001 APS/AAPM/ASAM guideline was published, the following manufacturers made the following payments to APS/AAPM/ASAM:

452.1. For example, in 2001, Purdue reportedly paid $211,211, Janssen paid approximately $159,000, and Endo paid $132,400 to APS.[914]

452.2. Likewise, Purdue paid $80,273, Janssen paid $66,764, and Endo paid $22,000 to AAPM in 2001.[915]

452.3. That same year, Endo paid $10,000 to ASAM.[916]

453. It appears that Endo may have influenced the final product,[917] and that Purdue was heavily involved in the development of these definitions. Dr. Haddox noted, "Purdue has been at the forefront of efforts to promote the proper therapeutic use of opioid analgesics, including funding the very first meeting of the AAPM/APS/ASAM leadership (when I was president of AAPM) to begin the collaboration that eventually led to the Consensus statement on definitions of pain and addiction."[918]

[913] PDD1502210202 at 254.

[914] *See* SFC00000001; END00000002; JAN00000001.

[915] END00000002; JAN00000001.

[916] ENDO-OPIOID_MDL-06234588; JAN00000001.

[917] *See* END00211516.

[918] PPLP003477086 at 24.

454. This guideline was used by opioid manufacturers in promoting their opioid products and opioids in general.[919]

3. APS Arthritis Guidelines

455. In 2002, the APS issued "Guidelines for the Management of Arthritis Pain," containing the following misleading statements:

455.1. "The prevalence of addiction among patients with pain who do not have a previously existing substance abuse disorder is low." [920]

455.2. "Weissman and Haddox (1989) noted that patients who are given doses of opioids that are inadequate to relieve their pain or whose opioid dose is discontinued abruptly or tapered too rapidly may develop characteristics that resemble addiction, which they termed iatrogenic 'pseudoaddiction.'"[921]

455.3. "Tolerance to analgesia is uncommon once pain relief has been achieved and there is no progression of disease." [922]

455.4. "Opioids should be used for patients with OA and RA when other medications and nonpharmacologic interventions produce inadequate pain relief and the patient's quality of life is affected by the pain."[923]

455.5. "Extensive experience and evidence in the management of chronic malignant pain supports the use of long-acting opioids to improve patient adherence, minimize medication level peaks and valleys, and minimize side effects. These

[919] *See, e.g.*, END00212229; ENDO-OPIOID MDL-01997737; ENDO-OPIOID_MDL-02939611 at 68; END00212229; ABT-MDL-KY-0009437 at 54.

[920] PKY181215749 at 95.

[921] PKY181215749 at 95.

[922] PKY181215749 at 96.

[923] PKY181215749 at 97.

increase in inappropriate use of opioids, all of which in turn increased the risk of opioid abuse and contributed to a public health crisis.

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